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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/694,579	10/27/2003	Jayesh Mehta	01017/39555	3753

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EXAMINER	
GALVEZ, JAMES JASON	
ART UNIT	PAPER NUMBER
1647	

DATE MAILED: 10/20/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/694,579	MEHTA ET AL.	
	Examiner	Art Unit	
	J. Jason Galvez	1647	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *28 September 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-10* is/are pending in the application.

4a) Of the above claim(s) *8* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-7,9 and 10* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *9/03/04*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

Applicant's election with traverse of Group I in the reply filed on 9/28/2004 is acknowledged. The traversal is on the ground(s) that searching the inventions together would not impart a search burden on the Examiner. This is not found persuasive because the inventions are directed to two distinct inventions and would impose a burden on the Examiner and USPTO resources. The Examiner maintains the inventions are distinct and not searchable together because searches for methods, for example Group I, and products, for example Group II, would require different search strategies and terms and are therefore not coextensive. In addition, the inventions are classified separately, which further supports the fact that the inventions are distinct and that searching the inventions together would impose a search burden on the Examiner and USPTO resources.

The requirement is still deemed proper and is therefore made FINAL.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1 and 5 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method of improving wall thickness following

ischemia and reperfusion, does not reasonably provide enablement for a method of reducing all forms of heart damage following ischemia and reperfusion. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims.

Claim 1 is drawn to a method of an improved reperfusion therapy whereby a reduction in "heart damage" is claimed. The recitation of "heart damage" has been interpreted by the Examiner to mean all forms of heart damage. Under the current interpretation, the broad claim of "heart damage" is not fully supported by the disclosure. Heart damage may encompass many aspects ranging from infarct size to damaged cellular components within the electron transport chain of mitochondria. Applicant has only disclosed the ability of the claimed method to improve wall thickness following ischemia and reperfusion. Therefore, it would not be possible to practice the claimed invention commensurate in scope due to the quantity of experimentation necessary, the lack of an adequate number and representative working examples, and the breadth of the claims.

In addition Applicant has claimed in claim 1 the administration of "an effective amount". The specification discloses an "effective amount" to be in the range of 0.001 μg/kg to 1000 μg/kg, preferably 300 μg per day. For the average person weighing 70 kg the dose per day would range from .07 μg to 70,000 μg. This range given for "effective amount" represents a 1 million-fold difference, which would never be considered an acceptable range when dealing with compositions and the use of compositions in

animal, and especially human, procedures. Therefore it would not be possible to use the invention commensurate in scope without experiments to support the broad range of concentrations in an "effective amount" due to the quantity of experimentation necessary, the lack of an adequate number and representative working examples, the nature of the invention, and the breadth of the claims

Claim 5 is drawn to a method of improved reperfusion therapy using a composition comprising of G-CSF and numerous cytokines that are proinflammatory, such as IL-8. Ischemia and reperfusion causes damage by promoting a non-specific inflammatory response. IL-8 is an inflammatory cytokine that is upregulated during ischemia and reperfusion, including coronary artery bypass (Vallely et al., The J Thoracic and Cardiovascular Surgery 2002, Vol 124(4): pp. 758-767, esp. Figure 1). The claimed invention is directed towards a method of increasing positive outcomes associated with ischemia and reperfusion, however molecules claimed to be used in the method to decrease damage to the heart may actually increase damage to the heart by increasing inflammation and consequently increasing tissue damage due to inflammatory processes.

In addition, none of cytokines recited in claim 5 were ever combined with G-CSF to show that this method would in fact display any protection against ischemia and reperfusion. As previously mentioned, there are a number of proinflammatory cytokines recited that would likely negate any protective effect of G-CSF. For the reasons stated above the expectation that the invention could be practiced with any degree of success is questionable. Therefore, it would not be possible to make and/or use the invention

commensurate in scope due to the quantity of experimentation necessary, the absence of an adequate number and representative working examples, the nature of the invention, the state of the prior art, and the predictability of the art.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Regarding claim 5, the phrase "includes the use of at least" renders the claim indefinite because it is unclear whether the limitation(s) following the phrase are part of an independent step or if the limitations following the phrase are supposed to co-administered simultaneously with G-CSF. See MPEP § 2173.05(d). It would be remedial to replace "includes the use of at least" with "includes ~~the use of~~ at least".

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1, 2, and 9 rejected under 35 U.S.C. 102(b) as being anticipated by Orlic et al. (PNAS 2001, Vol 98(18): pp.10344-10349). Orlic et al. teach that the use of G-CSF and SCF in conjunction (see p. 10344, column 2, lines 14-16) can positively influence myocardial outcomes following ischemia and reperfusion, such as improved wall thickness and increased ejection fraction when compared to untreated animals (see Figure 1 B-C and Figure 4 A-D).

Claims 1-7 and 9-10 are rejected under 35 U.S.C. 102(b) as being anticipated by Anversa (Pre-grant Patent Publication No. US 2002/0061587 A1 [05/2002]). Anversa teaches it is well know in the art that reperfusion therapy focuses on re-establishing blood flow through such methods as angioplasty, thrombolysis, and coronary bypass, however these methods have no effect on irreversibly damaged tissue (p. 2, paragraphs [0017-0018]). Anvera also teaches a method of reperfusion therapy comprising administering cytokines, including G-CSF, SCF, GM-CSF, IL-3, etc. (p. 1, paragraph [005]).

This method can be taken to be an improvement over standard procedures geared solely as re-establishing blood flow because the method and compositions claimed by Anversa induce stem cell mobilization and migration, which will aid in the regenerative process of the heart following ischemia and reperfusion (p.3, paragraph [038]). This is an important point because heart tissue is terminally differentiated and thus does not regenerate itself once critically injured. The method taught by Anversa showed protection against ischemia and reperfusion in the heart, as evidenced by improved wall thickness (Figure 13 A-B, Figure 15 A-C, and Figure 16 A-D). Anversa also teaches particular doses, 50 μg/kg to 500 μg/kg, that are claimed in the instant invention (p. 8, paragraph [0097]). Finally, Anversa teaches the method can be used on any vertebrate, including humans (p. 9, paragraph [0112]).

Conclusion

NO CLAIMS ALLOWED.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to **J. Jason Galvez, Ph.D.** whose telephone number is **571-272-2935**. The examiner can normally be reached Monday through Friday 9 AM to 5 PM. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, **Brenda Brumback, Ph.D.** can be reached at **571-272-0887**.

The fax phone number for the organization where this application or proceeding is assigned is **703-872-9306**. Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at **866-217-9197** (toll-free).

JJG
10/14/04

JANET ANDRES
PRIMARY EXAMINER